

IN THE CLAIMS:

CLAIMS

1) (Original) A method for the design and/or the selection of chemokines variants having agonist or antagonist property towards a ligand of GPCR of animal cells comprising the following steps:

- A) obtaining a phage displayed library expressing on their surface said chemokine variants mutated within the domain responsible for their effector function,
- B) having a culture of animal cells expressing on their membranes the GPCR,
- C) Incubating the cell culture with the phage library obtained in A),
- D) harvesting the cells after removal of non specifically bound and surface receptor bound phages,
- E) Releasing the phages internalized in step C) by lysis of cells obtained in D)
- F) Infecting an *E. coli* culture with the released phages obtained in E) and amplifying the clones previously internalized ,
- G) Obtaining a phage library enriched in internalizing chemokines ligands,
- H) Assaying the agonist or antagonist property of the chemokine variants versus the native one.

2) (Original) The method according to claim 1 wherein the chemokine is RANTES.

3) (Original) The method according to claim 1 wherein the GPCR expressed within the membrane of animal cells is CCR5.

4) (Original) The method according to claim 1 wherein the animal cells are human cells.

5) (Original) The method according to claim 2 wherein the phage library of RANTES variants is obtained using a method comprising the following steps:

- Obtaining a DNA sequence coding for human RANTES resulting from the amplification of cDNA prepared from activated PBMCs,
- Performing a PCR mutagenesis of the 5'portion of the DNA sequence of RANTES using a specific downstream primer and a degenerate upstream primer containing recognition sites for restriction enzymes in order to insert the PCR amplification products into the phage display vector,
- Inserting the purified PCR products into a phage display vector,
- Production of the phage library by introducing the vector containing the purified PCR products into an *E. coli* culture.

6) (Original) The method according to claim 2 wherein anti-HIV activity is assayed.

7) (Original) A method for the design and/or the selection of chemokines having agonist or antagonist property towards a GPCR of animal cells comprising the following steps:

- A) obtaining a phage displayed library expressing on their surface said chemokine mutated within the domain responsible for their effector function,
- B) having a culture of animal cells expressing on their membranes the GPCR,
- C) Incubating the cell culture with the phage library obtained in A),
- D) Eliminating the non specifically bound phages from the cells, by a process keeping the specifically bound phages on the said receptor
- E) Incubating the cells obtained in D) with an *E. coli* culture and amplifying the clones being infected by the phages bound to the said receptor on animal cells,
- F) Obtaining a phage library enriched in externally bound phages,
- G) Assaying the agonist or antagonist property of the chemokine variants versus the native chemokine.

8) (Original) The method according to claim 7 wherein the chemokine is RANTES.

9) (Original) The method according to claim 7 wherein the GPCR expressed within the membrane of animal cells is CCR5.

10) (Original) The method according to claim 7 wherein the animal cells are human cells.

11) (Original) The method according to claim 8 wherein the phage library of RANTES variants is obtained using a method comprising the following steps:

- Obtaining a DNA sequence coding for human RANTES resulting from the amplification of cDNA prepared from activated PBMCs,
- Performing a PCR mutagenesis of the 5'portion of the DNA sequence of RANTES using a specific downstream primer and a degenerate upstream primer containing recognition sites for restriction enzymes in order to insert the PCR amplification products into the phage display vector,
- Inserting the purified PCR products into a phage display vector,
- Production of the phage library by introducing the vector containing the purified PCR products into an E. coli culture.

12) (Original) The method according to claim 8 wherein anti-HIV activity is assayed.

13) (Currently Amended) A compound obtainable by a method according to anyone of claims 1 to 12 of the following formula:

*SP#SSQ&&& (SEQ ID NO: 24) -RANTES(10-68), in which

- * is L or an aromatic residue,
- # is L, M ouV
- & is S, P, T or A.

14) (Currently Amended) The compound according to claim 13) having one of the following formulae :

LSPVSSQSSA	<u>(SEQ ID NO: 1) (P₁)</u>
FSPLSSQSSA	<u>(SEQ ID NO: 2) (P₂)</u>
LSPMSSQSPA	<u>(SEQ ID NO: 3)</u>
WSPLSSQSPA	<u>(SEQ ID NO: 4)</u>
WSPLSSQSSP	<u>(SEQ ID NO: 5)</u>
LSPQSSLSSS	<u>(SEQ ID NO: 6)</u>
ASSGSSQSTS	<u>(SEQ ID NO: 7)</u>
ISAGSSQSTS	<u>(SEQ ID NO: 8)</u>
RSPMSSQSSP	<u>(SEQ ID NO: 9)</u>
YSPSSSLAPA	<u>(SEQ ID NO: 10)</u>
MSPLSSQASA	<u>(SEQ ID NO: 11)</u>
ASPMSSQSSS	<u>(SEQ ID NO: 12)</u>
QSPLSSQAST	<u>(SEQ ID NO: 13)</u>
QSPLSSTASS	<u>(SEQ ID NO: 14)</u>
LSPLSSQSAA	<u>(SEQ ID NO: 15)</u>
GSSSSSQTPA	<u>(SEQ ID NO: 16)</u>
YSPLSSQSSP	<u>(SEQ ID NO: 17)</u>
FSSVSSQSSS,	<u>(SEQ ID NO: 18)</u>
VSTLSSPAST,	<u>(SEQ ID NO: 30)</u>
ASSFSSRAPP,	<u>(SEQ ID NO: 31)</u>
QSSASSSSSA,	<u>(SEQ ID NO: 32)</u>
QSPGSSWSAA,	<u>(SEQ ID NO: 33)</u>
QSPSSWSSS,	<u>(SEQ ID NO: 34)</u>
QSPLSSFTSS,	<u>(SEQ ID NO: 35)</u>
LSPQSSLSSS,	<u>(SEQ ID NO: 6)</u>
ASPQSSLPAA,	<u>(SEQ ID NO: 36)</u>
LSPVSSQSSA	<u>(SEQ ID NO: 1)</u>

15) (Currently Amended) The compound according to claim 13) having the formula: FSPLSSQSSA (SEQ ID NO: 2)-RANTES(10-68).

16) (Currently Amended) The compound according to claim 13) having the formula: LSPVSSQSSA (SEQ ID NO: 1)-RANTES (10-68).

17) (Currently Amended) A pharmaceutical composition which comprises of a compound having the formula *SP#SSQ&&& (SEQ ID NO: 24)-RANTES(10-68), in which

- * is L or an aromatic residue,
- # is L, M ouV
- & is S, P, T or A,

or a pharmaceutical salt thereof, in a mixture with one or more pharmaceutically acceptable excipient.

18) (Currently Amended) The composition of claim 17) in which the compound have the formula: LSPVSSQSSA (SEQ ID NO: 1)-RANTES(10-68).

19) (Currently Amended) The composition of claim 17) in which the compound have the formula: FSPLSSQSSA (SEQ ID NO: 2)-RANTES(10-68).

20) (Original) A method for preventing and/or inhibiting HIV infection in humans comprising a step of treatment with a composition of claim 18).

21) (Original) A method for preventing and/or inhibiting HIV infection in humans comprising a step of treatment with a composition of claim 19).

22) (Original) A method for preventing and/or curing inflammatory or malignant diseases in humans comprising a step of treatment with a composition of claim 13 or 14.